

## Supporting Information

### Discovery of Diverse Small-Molecule Inhibitors of Mammalian Sterile20-like Kinase 3 (MST3)

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**Table S1: DSF results for the screening of MST3 KD against the kinase inhibitor library from Selleck Chemicals.**

Compound	Kinase target	ΔTm (°C)	Std. Error (°C)
NU7441(KU-57788)	DNA-PK, PI3K	-2.76	0.04
XL-184 free base (Cabozantinib)	VEGFR, c-Met, Flt, Tie-2, c-Kit	-2.13	0.17
KU-55933	ATM	-1.83	0.09
MLN8237 (Alisertib)	Aurora Kinase	-1.76	0.10
MLN8054	Aurora Kinase	-1.76	0.08
A-769662	AMPK	-1.72	0.02
PI-103	DNA-PK, PI3K, mTOR	-1.59	0.06
KX2-391	Src	-1.57	0.11
Temsirolimus (Torisel)	mTOR	-1.50	0.12
Vatalanib dihydrochloride (PTK787)	VEGFR, c-Kit, Flt	-1.45	0.02
GSK1838705A	IGF-1, ALK	-1.44	0.05
WYE-125132	mTOR	-1.32	0.13
GSK2126458	PI3K, mTOR	-1.29	0.13
TG 100713	PI3K	-1.20	0.12
Wortmannin	PI3K	-1.18	0.30
Pazopanib HCl	VEGFR, PDGFR, c-Kit	-1.17	0.26
XL765	PI3K, mTOR	-1.15	0.20
OSI-027	mTOR	-1.14	0.12
CP-724714	EGFR, HER2	-1.14	0.05
CAY10505	PI3K	-1.12	0.03
ZSTK474	PI3K	-1.12	0.34
WYE-687	mTOR	-1.11	0.15
AG-490	JAK, EGFR	-1.10	0.06
TGX-221	PI3K	-1.08	0.31
TG100-115	PI3K	-1.08	0.23
Tie2 kinase inhibitor	Tie-2	-1.01	0.08
PCI-32765 (Ibrutinib)	Src	-1.00	0.06
AS-604850	PI3K	-0.98	0.05
AS703026	MEK	-0.97	0.26
CHIR-98014	GSK-3	-0.96	0.01
Triciribine (Triciribine phosphate)	Akt	-0.91	0.10
Masitinib (AB1010)	c-Kit, PDGFR, FGFR, FAK	-0.91	0.06
Palomid 529	PI3K	-0.89	0.08
PF-05212384 (PKI-587)	mTOR, PI3K	-0.89	0.24
PD98059	MEK	-0.88	0.12
WYE-354	mTOR	-0.88	0.10
AZD8330	MEK	-0.88	0.27
AZD8055	mTOR	-0.87	0.28
Tofacitinib citrate (CP-690550 citrate)	JAK	-0.86	0.14
SB590885	Raf	-0.83	0.03
BS-181 HCl	CDK	-0.82	0.08
AG-1478 (Tyrphostin AG-1478)	EGFR	-0.82	0.04
JNJ-38877605	c-Met	-0.80	0.13
ZM336372	Raf	-0.80	0.09
KU-60019	ATM	-0.78	0.15
AMG458	c-Met	-0.78	0.04
WP1066	JAK	-0.77	0.13
SGX-523	c-Met	-0.74	0.14
GSK1120212 (Trametinib)	MEK	-0.74	0.14

YM201636	PI3K	-0.72	0.04
KU-0063794	mTOR	-0.71	0.11
PD0325901	MEK	-0.71	0.04
A66	PI3K	-0.70	0.19
BMS-599626 (AC480)	EGFR, HER2	-0.70	0.08
AZD6244 (Selumetinib)	MEK	-0.69	0.12
INCB28060	c-Met	-0.69	0.08
TAK-733	MEK	-0.67	0.01
LY2228820	p38 MAPK	-0.66	0.11
Roscovitine (Seliciclib, CYC202)	CDK	-0.63	0.19
MK-2461	c-Met	-0.63	0.03
PF-04217903	c-Met	-0.63	0.12
PF-04691502	mTOR, PI3K, Akt	-0.63	0.13
SB 203580	p38 MAPK	-0.62	0.08
Deforolimus (Ridaforolimus)	mTOR	-0.57	0.08
SB 525334	TGF-beta/Smad	-0.55	0.10
AZD6482		-0.54	0.16
LY2603618 (IC-83)	Chk	-0.53	0.16
AZD2014	mTOR	-0.52	0.14
LY294002	PI3K	-0.52	0.09
Arry-380	HER2	-0.52	0.17
SB 431542	TGF-beta/Smad	-0.51	0.05
NVP-BSK805	JAK	-0.48	0.13
PIK-293	PI3K	-0.48	0.05
Golvatinib (E7050)	c-Met	-0.47	0.07
Motesanib Diphosphate	VEGFR, PDGFR, c-Kit	-0.47	0.04
ARQ 197 (Tivantinib)	c-Met	-0.46	0.06
Erlotinib HCl	EGFR	-0.46	0.06
Perifosine		-0.46	0.08
PH-797804	p38 MAPK	-0.44	0.17
Everolimus (RAD001)	mTOR	-0.41	0.05
PIK-93	PI3K, VEGFR	-0.38	0.01
IC-87114		-0.37	0.13
GDC-0941	PI3K	-0.36	0.11
MK-2206 dihydrochloride	Akt	-0.34	0.26
PIK-90	PI3K	-0.31	0.07
BYL719	PI3K	-0.31	0.15
NVP-BGT226	PI3K	-0.30	0.11
GDC-0980 (RG7422)	mTOR, PI3K	-0.28	0.16
Aurora A Inhibitor I	Aurora Kinase	-0.27	0.05
Indirubin	GSK-3	-0.22	0.12
Tandutinib (MLN518)	Flt	-0.21	0.10
CAL-101 (GS-1101)	PI3K	-0.20	0.22
GSK1904529A	IGF-1R	-0.20	0.07
PD153035 HCl	EGFR	-0.20	0.02
HMN-214	PLK	-0.19	0.04
AZ628	Raf	-0.19	0.04
Torin 2	mTOR	-0.18	0.18
ARRY334543	EGFR	-0.16	0.06
Rigosertib (ON-01910)		-0.14	0.06
AS-605240	PI3K	-0.12	0.03
NVP-BVU972	c-Met	-0.11	0.31

WAY-600	mTOR	-0.10	0.05
R788 (Fostamatinib)	Syk	-0.10	0.30
GSK1059615	PI3K, mTOR	-0.09	0.06
Imatinib Mesylate	PDGFR, c-Kit, Bcr-Abl	-0.06	0.30
AMG-208	c-Met	-0.05	0.12
R406	Syk, Flt	-0.03	0.18
WHI-P154	JAK	-0.02	0.07
Tofacitinib (CP-690550, Tasocitinib)	JAK	-0.01	0.05
GDC-0879	Raf	0.01	0.09
TG101348 (SAR302503)	JAK	0.03	0.06
TSU-68	VEGFR, PDGFR , FGFR	0.05	0.17
VX-702	p38 MAPK	0.05	0.14
Cyt387	JAK	0.08	0.01
Imatinib (Gleevec)	PDGFR	0.08	0.17
PIK-294	PI3K	0.09	0.02
AG-1024	IGF-1R	0.10	0.03
CH5424802	ALK	0.10	0.12
3-Methyladenine	PI3K	0.11	0.21
GSK461364	PLK	0.14	0.01
Piceatannol	Syk	0.14	0.01
Ruxolitinib (INCB018424)	JAK	0.14	0.08
Ki8751	VEGFR, c-Kit, PDGFR	0.16	0.10
Tyrphostin AG 879 (AG 879)	HER2	0.17	0.04
CCT128930	Akt	0.17	0.27
AT7519	CDK	0.18	0.11
Phenformin hydrochloride	AMPK	0.21	0.17
PD318088	MEK	0.21	0.04
BMS 777607	c-Met	0.23	0.07
AZD8931	EGFR, HER2	0.23	0.13
Apatinib (YN968D1)	VEGFR	0.24	0.03
Vandetanib (Zactima)	VEGFR	0.24	0.11
BMS-265246	CDK	0.25	0.21
Torin 1	mTOR	0.26	0.02
Telatinib (BAY 57-9352)	VEGFR, PDGFR, c-Kit	0.33	0.05
KRN 633	VEGFR, PDGFR	0.34	0.03
Baricitinib (LY3009104)	JAK	0.37	0.11
R406 (free base)	Syk	0.38	0.17
SB 216763	GSK-3	0.38	0.02
BEZ235 (NVP-BEZ235)	mTOR, PI3K	0.41	0.05
Y-27632 2HCl	ROCK	0.45	0.05
SCH 900776		0.49	0.01
BI 2536	PLK	0.49	0.11
PKI-402	PI3K	0.50	0.04
IMD 0354	IKK	0.53	0.08
cx-4945 (Silmitasertib)	PKC	0.55	0.01
MK-5108 (VX-689)	Aurora Kinase	0.57	0.02
TG101209	Flt, JAK, c-RET	0.58	0.10
Gefitinib (Iressa)	EGFR	0.60	0.01
AT7867	Akt, S6 kinase	0.65	0.09
WZ4002	EGFR	0.66	0.03
BIRB 796 (Doramapimod)	p38 MAPK	0.70	0.11
LDN193189	TGF-beta/Smad	0.71	0.10

OSI-930	c-Kit, VEGFR	0.71	0.04
Barasertib (AZD1152-HQPA)	Aurora Kinase	0.71	0.08
BKM120 (NVP-BKM120)	PI3K	0.74	0.32
CI-1033 (Canertinib)	EGFR, HER2	0.75	0.04
Enzastaurin (LY317615)	PKC	0.77	0.09
GDC-0068	Akt	0.77	0.07
PLX-4720	Raf	0.78	0.02
Dacomitinib (PF299804,PF-00299804)	EGFR	0.79	0.02
Mubritinib (TAK 165)	HER2	0.83	0.08
R935788 (Fostamatinib disodium, R788)	Syk	0.84	0.08
Thiazovivin	ROCK	0.90	0.09
Axitinib	VEGFR, PDGFR, c-Kit	0.91	0.13
SB 202190	p38 MAPK	0.94	0.03
Afatinib (BIBW2992)	EGFR, HER2	0.98	0.07
GSK1070916	Aurora Kinase	1.01	0.14
PHA-767491	CDK	1.07	0.04
CI-1040 (PD184352)	MEK	1.12	0.02
NVP-ADW742	IGF-1R	1.14	0.10
BIX 02189	MEK	1.17	0.22
BGJ398 (NVP-BGJ398)	FGFR	1.17	0.08
ZM-447439	Aurora Kinase	1.18	0.04
BI6727 (Volasertib)	PLK	1.18	0.21
NVP-TAE226	FAK	1.21	0.09
BIX 02188	MEK	1.21	0.26
CYC116	Aurora Kinase, VEGFR	1.32	0.07
OSI-420 (Desmethyl Erlotinib)	EGFR	1.38	0.06
Flavopiridol hydrochloride	CDK	1.39	0.05
SNS-032 (BMS-387032)	CDK	1.40	0.07
SP600125	JNK	1.42	0.04
TWS119	GSK-3	1.45	0.06
CCT137690	Aurora Kinase	1.46	0.06
INK 128	mTOR	1.48	0.31
SAR131675	VEGFR	1.51	0.24
Tideglusib	GSK-3	1.54	0.06
AEE788 (NVP-AEE788)	EGFR, Flt, VEGFR, HER2	1.55	0.11
Saracatinib (AZD0530)	Src, Bcr-Abl	1.64	0.17
Brivanib alaninate (BMS-582664)	VEGFR	1.68	0.04
BMS 794833	c-Met, VEGFR	1.68	0.13
Brivanib (BMS-540215)	VEGFR	1.71	0.04
NVP-BHG712	VEGFR, Src, Raf, Bcr-Abl	1.73	0.03
KW 2449	Flt, Bcr-Abl, Aurora Kinase	1.77	0.09
SNS-314	Aurora Kinase	1.79	0.01
PD 0332991 (Palbociclib) HCl	CDK	1.80	0.07
Dabrafenib (GSK2118436)	Raf	1.83	0.21
Dasatinib (BMS-354825)	Src, Bcr-Abl, c-Kit	1.83	0.06
Desmethyl Erlotinib (CP-473420)	EGFR	1.86	0.13
E7080 (Lenvatinib)	VEGFR	1.87	0.02
Linifanib (ABT-869)	PDGFR, VEGFR	1.92	0.04
Foretinib (GSK1363089, XL880)	c-Met, VEGFR	2.00	0.03
GSK690693	Akt	2.02	0.11
CEP33779	JAK	2.04	0.08
BX-795	PDK-1	2.06	0.05

Crizotinib (PF-02341066)	c-Met, ALK	2.19	0.06
AZ 960	JAK	2.21	0.02
U0126-EtOH	MEK	2.44	0.02
SB 415286	GSK-3	2.47	0.03
Linsitinib (OSI-906)	IGF-1R	2.51	0.10
VX-680 (MK-0457, Tozastertib)	Aurora Kinase	2.65	0.04
PP242	mTOR	2.73	0.02
ENMD-2076	Flt, Aurora Kinase, VEGFR	2.76	0.06
TAK-901	Aurora Kinase	2.77	0.05
PHA-665752	c-Met	2.87	0.12
TAE684 (NVP-TAE684)	ALK	2.91	0.05
TAK-285	EGFR	2.91	0.01
LY2784544	JAK	2.92	0.02
WZ3146	EGFR	2.98	0.06
TPCA-1	IKK	3.06	0.06
CCT129202	Aurora Kinase	3.07	0.05
WZ8040	EGFR	3.11	0.02
Quercetin (Sophoretin)	PI3K, PKC, Src, Sirtuin	3.30	0.03
Cediranib (AZD2171)	VEGFR, Flt	3.49	0.09
PHA-848125	CDK	3.51	0.12
AZD5438	CDK	3.73	0.27
Dinaciclib (SCH727965)	CDK	3.86	0.03
BX-912	PDK-1	3.94	0.05
A-674563	Akt, CDK, PKA	4.05	0.02
AZD7762	Chk	4.08	0.02
JNJ-7706621	CDK, Aurora Kinase	4.23	0.07
PHA-680632	Aurora Kinase	4.33	0.19
AZD4547	FGFR	4.49	0.10
PD173074	FGFR	4.61	0.15
Ponatinib (AP24534)	Bcr-Abl, VEGFR, FGFR, PDGFR, Flt	4.63	0.03
AT9283	Bcr-Abl, JAK, Aurora Kinase	4.84	0.05
Dovitinib (TKI-258)	FLT3	4.95	0.05
Dovitinib Dilactic acid (TKI258 Dilactic acid)	FLT3	5.03	0.04
Sunitinib Malate (Sutent)	VEGFR, PDGFR, c-Kit, Flt	5.05	0.11
Pelitinib (EKB-569)	EGFR	5.18	0.01
PHA-793887	CDK	5.19	0.08
PP-121	DNA-PK, mTOR, PDGF	5.26	0.08
PF-00562271	FAK	5.73	0.06
Danusertib (PHA-739358)	Aurora Kinase, FGFR, Bcr-Abl, c-RE	6.06	0.05
Sotрастaurин (AEB071)	PKC	6.28	0.05
Crenolanib (CP-868569)	PDGFR	7.07	0.10
CP 673451	PDGFR	7.41	0.13
Neratinib (HKI-272)	HER2, EGFR	7.50	0.01
PF-03814735	Aurora Kinase	7.58	0.08
Bosutinib (SKI-606)	Src	7.69	0.01
CHIR-124	Chk	7.94	0.06
BIBF1120 (Vargatef)	VEGFR, PDGFR, FGFR	8.13	0.01
Hesperadin	Aurora Kinase	9.08	0.11
Staurosporine	PKC	10.80	0.08
Tivozanib (AV-951)	VEGFR, c-Kit, PDGFR	Compound interference w/ signal	
Raf265 derivative	VEGFR, Raf	Compound interference w/ signal	
OSU-03012	PDK-1	Compound interference w/ signal	

Se�axanib (SU5416)	VEGFR	Compound interference w/ signal
Amuvatinib (MP-470)	c-Met, c-Kit, PDGFR, Flt, c-RET	Compound interference w/ signal
Sorafenib (Nexavar)	VEGFR, PDGFR, Raf	Compound interference w/ signal
MGCD-265	c-Met, VEGFR, Tie-2	Compound interference w/ signal
Nilotinib (AMN-107)	Bcr-Abl	Compound interference w/ signal
PIK-75 Hydrochloride	PI3K, DNA-PK	Compound interference w/ signal
Quizartinib (AC220)	Flt	Compound interference w/ signal
Rapamycin (Sirolimus)	mTOR	Compound interference w/ signal
AMG900	Aurora Kinase	Compound interference w/ signal
Regorafenib (BAY 73-4506)	c-Kit, Raf, VEGFR	Compound interference w/ signal
PHT-427	Akt	Compound interference w/ signal
SU11274	c-Met	Compound interference w/ signal
Lapatinib Ditosylate (Tykerb)	EGFR, HER2	Compound interference w/ signal
DCC-2036 (Rebastinib)	Bcr-Abl	Compound interference w/ signal
RAF265 (CHIR-265)		Compound interference w/ signal
WP1130	DUB, Bcr-Abl	Compound interference w/ signal
XL147	PI3K	Compound interference w/ signal
AS-252424	PI3K	Compound interference w/ signal
Vemurafenib (PLX4032)	Raf	Compound interference w/ signal
AST-1306	EGFR	Compound interference w/ signal

**Table S2: Crystallographic data collection and refinement statistics.**

Lig # <sup>a</sup>	Ligand name	PDB ID	Ligand PDB ID	Space group	Data Collection							Structure Refinement															
					Cell dimensions					resolution range		Unique reflections		Rsym <sup>b</sup> (%)	Completeness (%)		I/oI	Rcryst <sup>c</sup> (%)	Rfree <sup>d</sup> (%)	Average B all <sup>e</sup> (Å)	Average B protein <sup>f</sup> (Å)	Average B ligand <sup>g</sup> (Å)	Average B solvent <sup>h</sup> (Å)	Wilson B (Å)	rmsd <sup>i</sup> bonds (Å)	rmsd <sup>i</sup> angles (deg)	Coordinate Error (Å)
1	ANP-PNP	4QML	ANP	P 2 <sub>1</sub>	47.53	55.12	60.88	90.00	112.67	90.00	1.88-20.00 (1.88-1.91)	23,571 (1,010)	3.5 (28.8)	99.0 (83.1)	44.1 (5.4)	19.0	23.0	35.0	34.9	36.0	36.8	30.0	0.008	1.16	0.18	97.49	2.15
2	AT9283	4QMM	34R	C 2	99.65	58.64	61.79	90.00	94.11	90.00	1.85-20.00 (1.85-1.88)	29,959 (1,306)	3.5 (18.8)	98.9 (87.5)	41.9 (4.6)	14.1	19.8	32.5	32.2	34.6	35.4	24.4	0.006	1.02	0.16	97.21	2.44
3	Bosutinib	4QMN	D88	P 2 <sub>1</sub>	47.42	55.36	60.44	90.00	111.32	90.00	2.09-20.00 (2.09-2.13)	17,405 (850)	4.9 (20.6)	99.8 (97.0)	38.5 (9.0)	17.1	22.5	27.6	27.5	28.6	28.5	24.8	0.008	1.12	0.23	95.41	4.24
4	C16	4QMO	34L	C 2	99.35	58.74	61.64	90.00	93.44	90.00	1.90-20.00 (1.90-1.93)	27,646 (1,357)	4.4 (38.8)	98.4 (96.0)	37.7 (5.5)	16.5	20.4	30.7	30.2	27.4	35.1	26.3	0.007	1.07	0.20	97.57	2.43
5	CDK1/2 Inhibitor III	4QMP	DKI	C 2	99.44	57.45	61.54	90.00	93.66	90.00	2.00-20.00 (2.00-2.10)	23,474 (3,178)	3.9 (33.6)	99.6 (99.8)	21.7 (3.8)	17.8	22.8	35.6	35.6	30.2	36.5	29.9	0.008	1.08	0.19	96.53	2.78
6	CP-673451	4QMQ	34U	C 2	99.48	58.36	61.72	90.00	93.21	90.00	1.77-20.00 (1.77-1.80)	34,556 (1,722)	4.8 (31.7)	100.0 (100.0)	33.0 (3.8)	18.9	22.3	28.1	28.3	20.5	27.8	22.8	0.007	1.07	0.18	97.20	2.80
7	Danusertib	4QMR	627	P 2 <sub>1</sub>	53.63	90.72	61.88	90.00	92.89	90.00	2.20-20.00 (2.20-2.26)	29,718 (2,154)	7.7 (33.3)	98.8 (98.4)	17.1 (4.5)	16.0	21.1	24.0	23.9	24.4	24.4	19.6	0.008	1.15	0.22	96.80	3.20
8	Dasatinib	4QO9	1N1	P 2 <sub>1</sub>	47.49	55.13	60.24	90.00	111.35	90.00	1.88-20.00 (1.88-1.91)	23,554 (1,005)	7.8 (14.3)	99.2 (85.3)	47.3 (14.1)	16.9	21.4	20.4	20.1	24.6	23.4	17.9	0.007	1.15	0.17	96.82	2.83
9	Hesperadin	4QMT	H1N	P 21	47.88	55.34	60.34	90.00	111.63	90.00	1.50-20.00 (1.50-1.53)	46,965 (2,309)	5.0 (32.5)	99.9 (100.0)	30.1 (3.3)	15.1	18.6	22.3	21.6	23.5	28.9	15.3	0.006	1.07	0.15	97.17	2.47
10	TP fragment	4QNA	X11	P 2 <sub>1</sub>	47.32	54.78	60.18	90.00	111.45	90.00	1.85-20.00 (1.85-1.88)	23,257 (1,116)	9.4 (30.3)	94.4 (91.4)	29.0 (2.7)	18.0	21.5	35.4	35.2	39.1	37.3	31.5	0.007	1.11	0.22	95.05	4.95
11	JNJ-7706621	4QNU	SKE	P 2 <sub>1</sub>	47.69	54.81	60.52	90.00	111.78	90.00	1.55-20.00 (1.55-1.58)	41,913 (1,909)	4.1 (21.1)	99.1 (91.4)	42.5 (4.5)	17.8	20.6	20.6	20.2	16.2	26.4	17.7	0.006	1.11	0.14	97.55	2.45
12	PF-03814735	4QMV	34W	C 2	100.08	57.85	61.78	90.00	93.98	90.00	2.40-20.00 (2.40-2.46)	13,859 (982)	5.2 (31.5)	99.5 (99.8)	21.9 (4.3)	16.7	22.6	34.3	34.5	34.1	30.5	31.6	0.008	1.19	0.30	97.21	2.79
13	PP-121	4QMW	K51	P 2 <sub>1</sub>	47.76	55.24	60.23	90.00	111.01	90.00	1.60-20.00 (1.60-1.62)	38,266 (1,726)	3.8 (17.7)	98.7 (88.3)	37.5 (4.8)	17.7	21.1	20.6	20.2	16.2	25.2	16.2	0.006	1.18	0.14	96.50	3.50
14	Saracatinib	4QMX	H8H	P 2 <sub>1</sub>	47.55	55.12	60.64	90.00	111.58	90.00	1.90-20.00 (1.90-1.93)	22,568 (1,079)	4.7 (23.3)	97.6 (95.9)	42.3 (8.8)	17.9	21.9	25.0	24.8	32.3	26.1	22.4	0.007	1.09	0.21	96.85	3.15
15	Staurosporine	4QMY	STU	P 2 <sub>1</sub>	47.44	54.79	60.88	90.00	111.63	90.00	1.90-20.00 (1.90-1.93)	27,646 (1,357)	4.4 (38.8)	98.4 (96.0)	37.6 (5.5)	18.0	22.0	32.0	31.9	32.6	37.5	25.9	0.007	1.12	0.21	95.45	4.20
16	Sunitinib	4QMZ	B49	P 2 <sub>1</sub>	47.79	55.30	60.66	90.00	111.50	90.00	1.88-20.00 (1.88-1.91)	23,687 (1,038)	3.8 (10.5)	98.0 (86.4)	54.3 (22.8)	16.8	22.4	27.1	36.7	32.2	30.1	23.4	0.007	1.09	0.20	95.79	4.21

<sup>a</sup>Ligands sorted alphabetically

<sup>b</sup>Rsym = 100  $\times \frac{\sum h\bar{h} - \langle h \rangle \langle \bar{h} \rangle}{\sum h\bar{h}}$  where h are unique reflection indices.

<sup>c</sup>Rcryst = 100  $\times \frac{\sum |F_{\text{obs}} - F_{\text{model}}|}{\sum F_{\text{obs}}}$

<sup>d</sup>Rfree is Rcryst calculated for randomly chosen unique reflections.

<sup>e</sup>Excluding hydrogen atoms

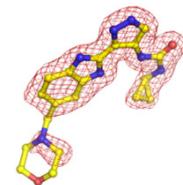
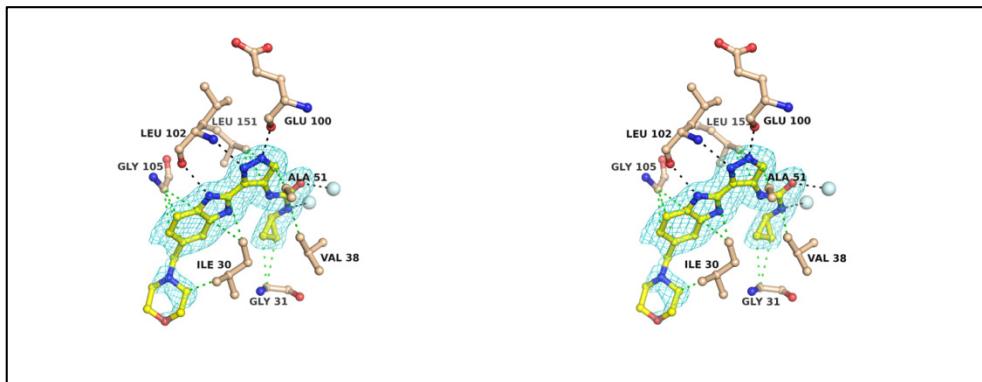
<sup>f</sup>Rmsd = root-mean-square deviation from ideal values, which were excluded from the refinement.

**Table 3: Comparison of melting temperature shifts between full-length (FL) and kinase domain (KD) of MST3**

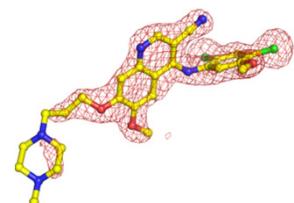
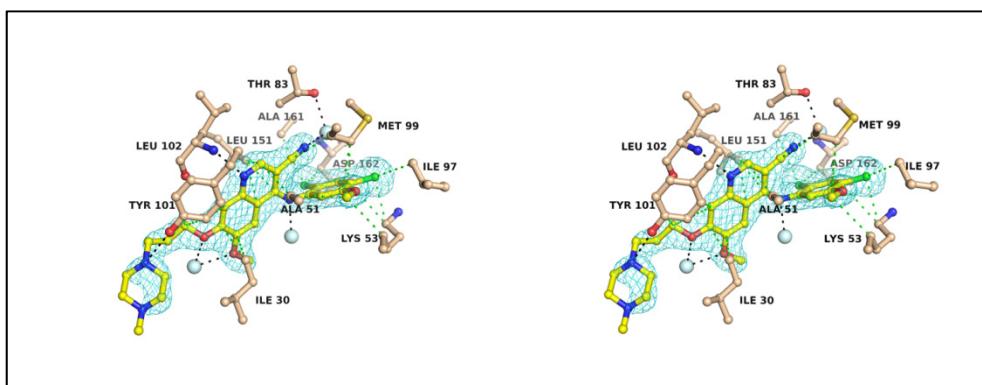
Ligand	MST3 FL		MST3 KD	
	dTm	Std. Error	dTm	Std. Error
ADP	0.5	0.04	0.1	0.22
AMP-PNP	0.4	0.22	0.2	0.20
AMP-PNP	0.5	0.08	0.3	0.24
Bosutinib	9.4	0.05	8.3	0.06
C16	7.8	0.06	7.7	0.07
Dasatinib	2.7	0.07	3.1	0.05
DMSO	0.0	0.14	0.0	0.14
DMSO	0.0	0.12	0.0	0.12
Inhibitor III	10.2	0.02	9.6	0.07
Inhibitor III	11.1	0.05	10.1	0.11
L2	1.3	0.06	1.0	0.01
Saracatinib	3.3	0.13	2.4	0.10
Saracatinib	3.6	0.05	3.0	0.09
Staurosporine	13.3	0.10	12.3	0.06
Sunitinib	6.9	0.09	6.9	0.05

**Figure S1: Detailed binding interactions of inhibitors with the ATP site of MST3 (stereo presentations).** Ligand is shown in yellow and the corresponding 2Fo-Fc electron density map is shown as blue mesh (contoured at 1 $\sigma$ ). Protein residues are colored in beige and water molecules are displayed as cyan spheres. Hydrogen bonding interactions are indicated as black dotted lines and VDW interactions (hydrophobic) as green dotted line. The Fo-Fc electron density maps omitting the inhibitor is shown as red mesh (contoured at 3 $\sigma$ ) as insert.

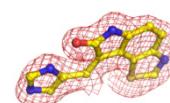
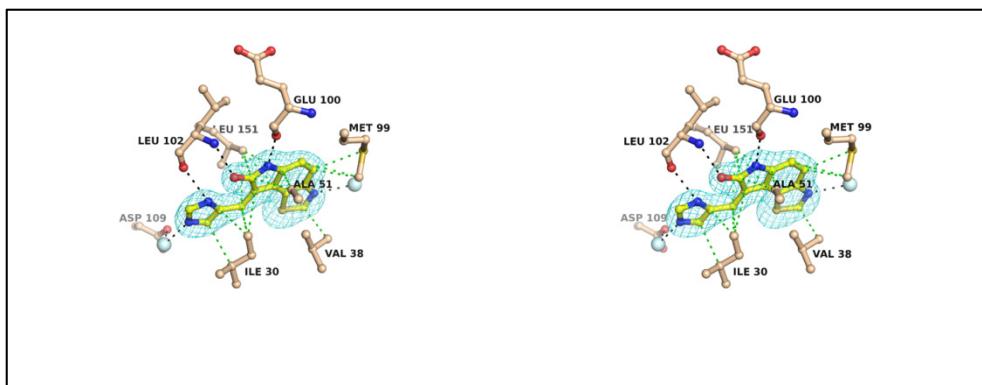
**AT9283**



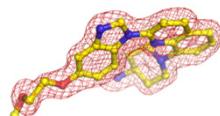
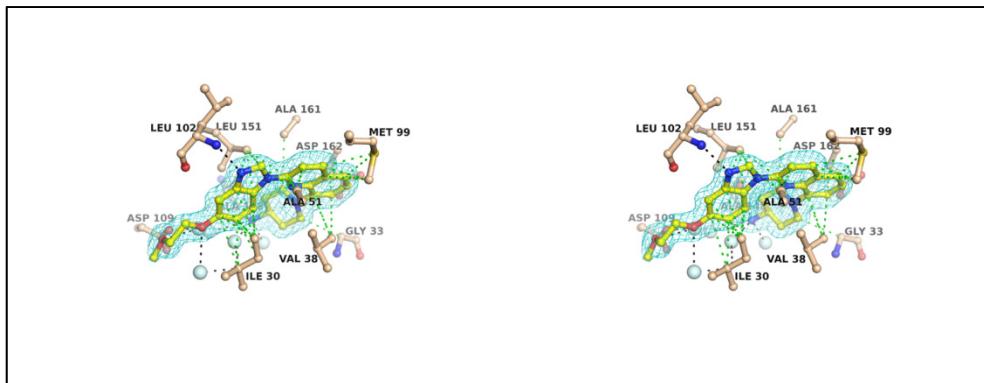
**Bosutinib**



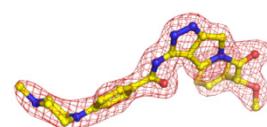
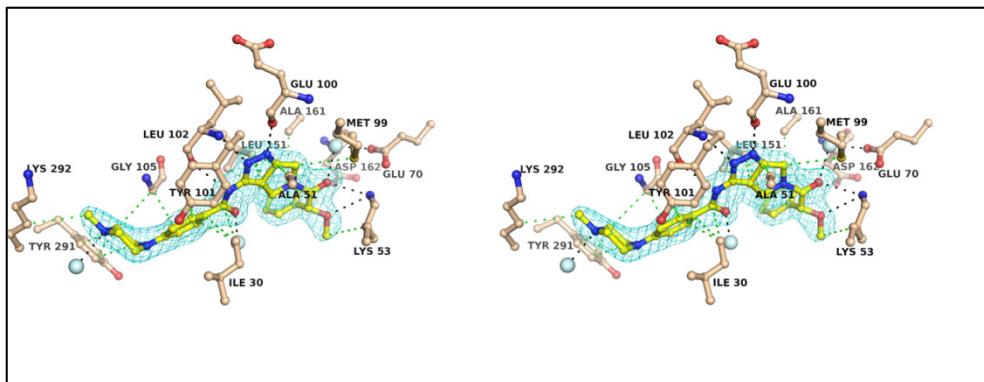
**Imidazolo-oxindole PKR inhibitor C16**



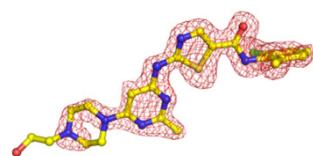
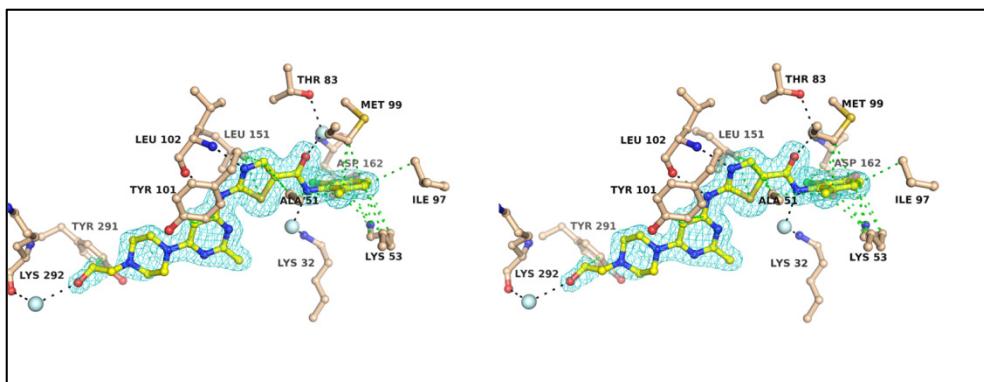
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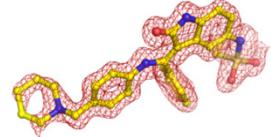
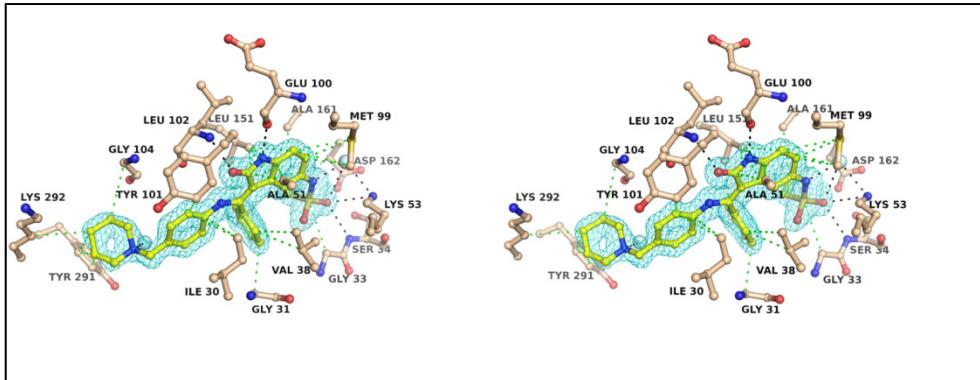
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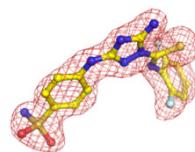
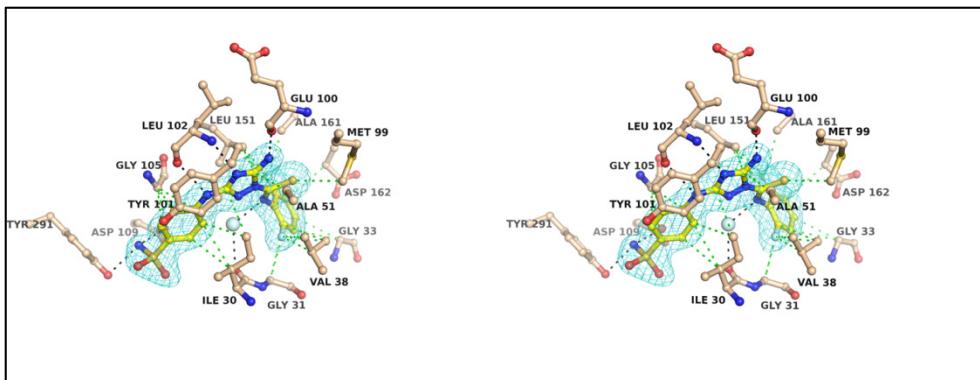
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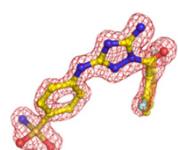
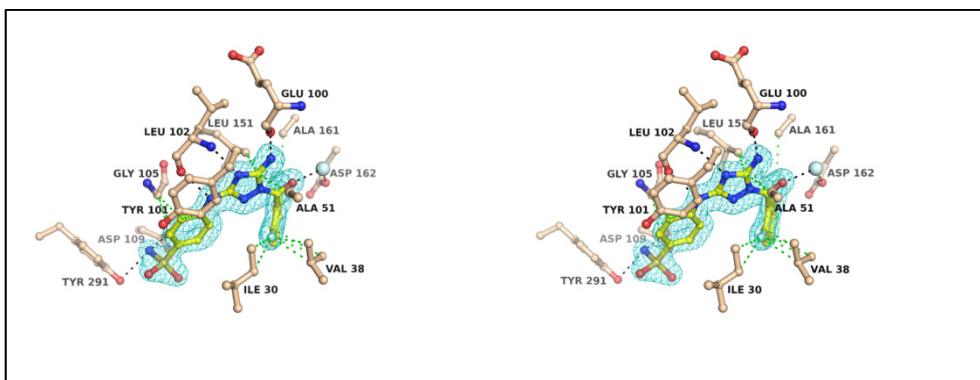
### Hesperadin



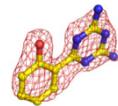
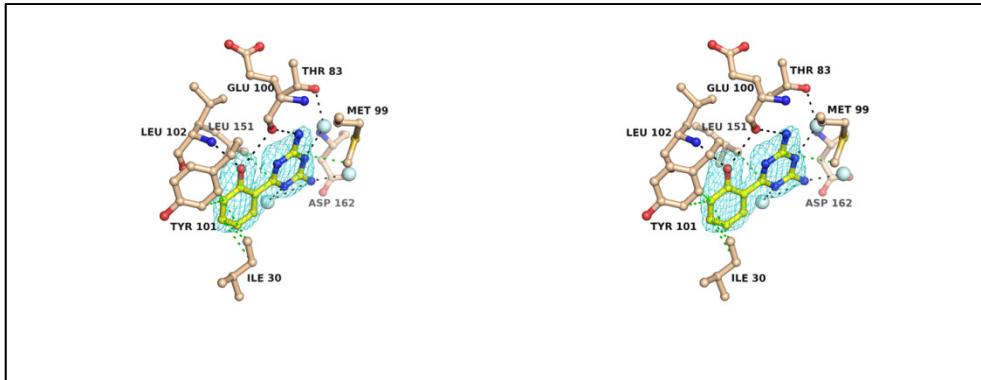
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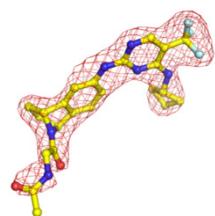
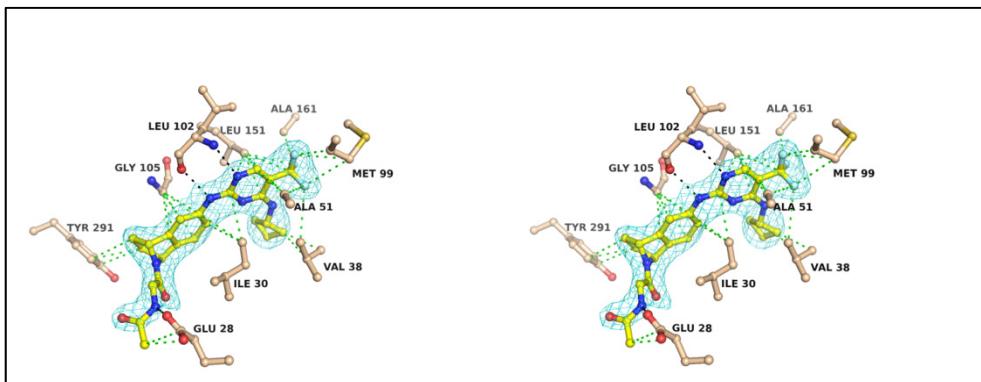
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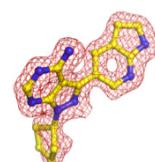
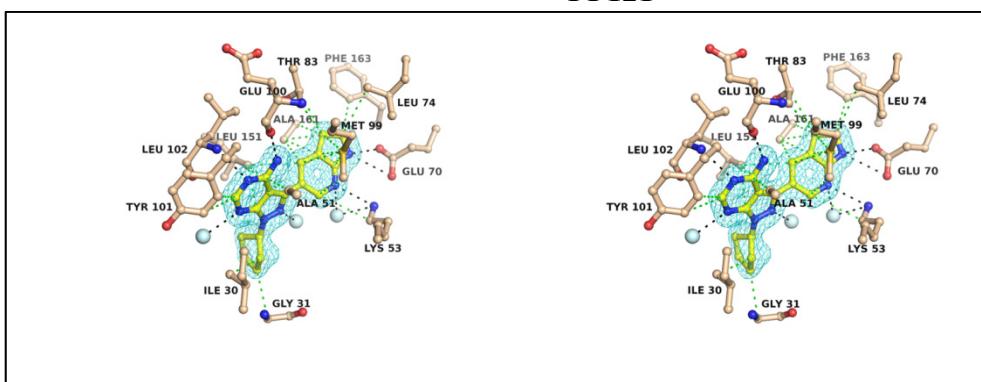
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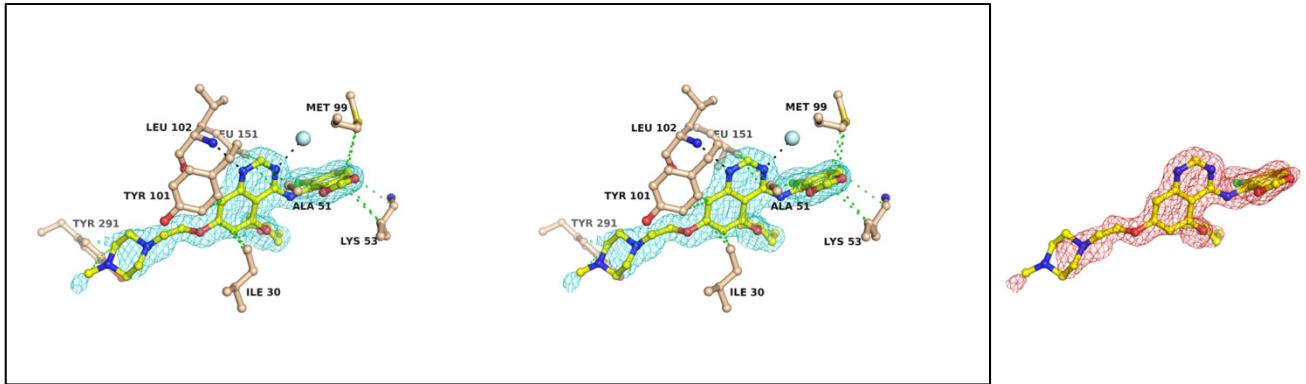
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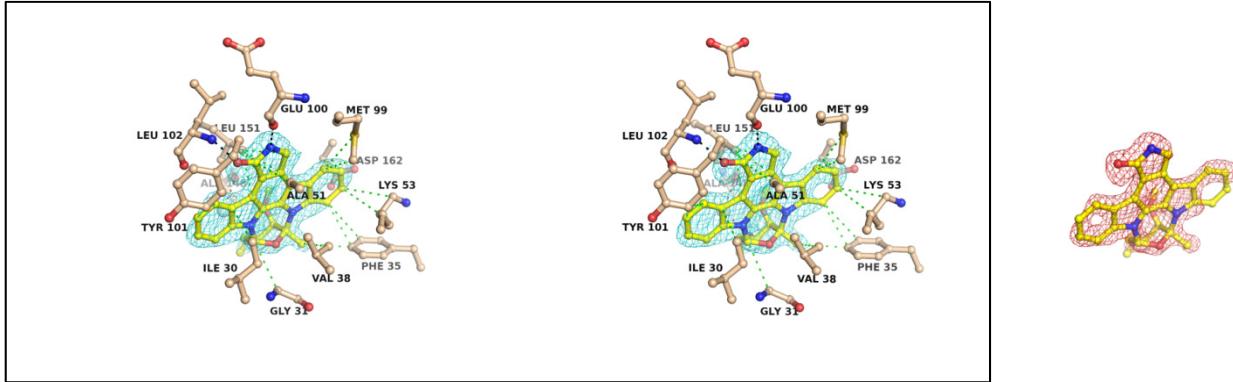
### PP121



### Saracatinib



### Staurosporine



### Sunitinib

